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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/851,628	05/06/1997	CHARLES M. COHEN	JJJ-PO1-515	6154

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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/851,628	COHEN ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-10,12,15-17,24,28,32 and 52-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10,12,15-17,24,28,32 and 52-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-4,6-10,12,15-17,24,28,32 and 52-55* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *38* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed May 9, 2003 (Paper No. 41) has been entered. Claims 1-4, 6-10, 12, 15-17, 24, 28, 32, 52-55 are pending. Claims 1-4, 6-10, 12, 15-17, 24, 28, 32, 52-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), to the extent that they are drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 36. Claims 1-4, 6-10, 12, 15-17, 24, 28, 32, 52-55 are being examined to the extent that they read upon the species the mature form of OP1, MRI, and chronic diabetic nephropathy.

Maintained Formal Matters, Objections, and/or Rejections:

Double Patenting

Claims 1-4, 6-10, 12, 15-17, 24, 28, 32, 52-55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 6,498,142 . It is acknowledged that Applicant will file a terminal disclaimer upon the notification of allowable subject matter and that Applicant contends that nothing is necessary at this time.

Claim Rejections - 35 USC § 103

Claims 1-4, 6-10, 12, 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath (BB, cited by Applicants), Watanabe (x18), and Glassock (v6).

Claims 1, 2, 15, 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath (BB, cited by Applicants), Watanabe (x18), and Glassock (v6) as applied to claims 1, 2 above, and further in view of Coe (z18), Kees-Folts (y18), and Jennerholm (u37).

Claims 1, 2, 17, 24, 28, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath (BB, cited by Applicants), Watanabe (x18), and Glassock (v6) as applied to claims 1, 2 above, and further in view of Brenner (u18).

Applicant argues:

that the rejection does not establish a prima facie case of obviousness with respect to the invention as recited in the claims (see paragraph bridging pages 7-8 of the response);

that the rejection does not provide any rationale for why the combination of the cited references renders obvious either "(1)" or "(2)" (see page 8, full paragraph 1, of the response;

that the rejection does not provide a sufficient motivation to combine the references (see page 8, full paragraph 2, of the response);

that there is no suggestion in the cited references to use a morphogen to treat chronic renal failure and chronic diabetic nephropathy (see paragraph bridging pages 8-9 of the response;

that the rejection does not provide a reasonable expectation of success for using a morphogen to treat to treat chronic renal failure and chronic diabetic retinopathy (see paragraph bridging pages 8-9 of the response);

that rejection uses impermissible hindsight reconstruction of Applicant's invention (see paragraph bridging pages 8-9 of the response).

Applicant's arguments have been fully considered but they are not persuasive.

There are six embodiments (two embodiments in claim 1 and four in claim 2) in the alternative to the presents claims with respect to the mammal and pathology treated, as follows:

1.a. A method of improving renal function in a mammal in chronic renal failure, wherein said mammal is afflicted with a chronic renal condition characterized by the progressive loss of renal function associated with the progressive loss of functioning nephron units, wherein said chronic renal condition is chronic diabetic nephropathy.

1.b. A method of improving renal function in a mammal at risk of chronic renal failure, wherein said mammal is afflicted with a chronic renal condition characterized by the progressive loss of renal function associated with the progressive loss of functioning nephron units, wherein said chronic renal condition is chronic diabetic nephropathy.

2.a. A method of delaying the need for chronic dialysis treatments in a mammal in chronic renal failure, wherein said mammal is afflicted with a chronic renal condition characterized by the progressive loss of renal function associated with the progressive loss of functioning nephron units, wherein said chronic renal condition is chronic diabetic nephropathy.

2.b. A method of reducing the frequency of chronic dialysis treatments in a mammal in chronic renal failure, wherein said mammal is afflicted with a chronic renal condition characterized by the progressive loss of renal function associated with the progressive loss of functioning nephron units, wherein said chronic renal condition is chronic diabetic nephropathy.

2.c. A method of delaying the need for chronic dialysis treatments in a mammal at risk of chronic renal failure, wherein said mammal is afflicted with a chronic renal condition characterized by the progressive loss of renal function associated with the progressive loss of functioning nephron units, wherein said chronic renal condition is chronic diabetic nephropathy.

2.d. A method of reducing the frequency of chronic dialysis treatments in a mammal at risk of chronic renal failure, wherein said mammal is afflicted with a chronic renal condition characterized by the progressive loss of renal function associated with the progressive loss of functioning nephron units, wherein said chronic renal condition is chronic diabetic nephropathy.

If any one of these embodiments is taught by the prior art then the claim encompassing that embodiment is properly rejected in view of the prior art.

If the prior provides a teaching, suggestion, or motivation to treat chronic diabetic nephropathy with OP-1 then the prior art teaches administering OP-1 to a mammal afflicted with "a chronic renal condition characterized by the progressive loss of renal function associated with the progressive loss of functioning nephron units" because, according to the present claims, chronic diabetic nephropathy is "a chronic renal condition characterized by the progressive loss of renal function associated with the progressive loss of functioning nephron units."

All mammals, including those with chronic diabetic retinopathy and those without, are "at risk of chronic renal failure." It follows then that treating chronic diabetic nephropathy with OP-1 would improve renal function in a mammal afflicted with chronic diabetic nephropathy, in the absence of evidence to the contrary, because there is no difference in the presently claimed method steps and the method steps taught by the prior art and a prima facie case of obviousness has been established.

Assuming then that the prior art teaches administering OP-1 to a mammal afflicted with chronic diabetic nephropathy then it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat such a mammal whether or not such a mammal was "in chronic renal failure" because one of ordinary

skill in the art would be motivated to treat the underlying pathology, i.e., chronic diabetic retinopathy.

The limitation "delaying the need for chronic dialysis treatments" does not require that the mammal be undergoing dialysis.

The limitation "reducing the frequency of chronic dialysis treatments" implies that the mammal is undergoing dialysis. However, if it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat chronic diabetic nephropathy with OP-1 it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat such a mammal whether or not such a mammal was undergoing dialysis because it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat the underlying pathology, i.e., chronic diabetic retinopathy.

Kuberasampath (BB, cited by Applicants) teaches that damage to cells resulting from the effects of inflammatory response has been implicated as the cause of reduced tissue function or loss of tissue function in diseases of the kidney. For example, glomerular nephritis and diabetes are believed to result in large part from unwanted acute inflammatory reaction and fibrosis. See paragraph bridging pages 1-2. The immune cell mediated tissue destruction often follows an initial tissue injury or insult; the secondary damage often is the source of significant tissue damage. Humoral agents that mediate tissue damage are produced by adhering neutrophilic leukocytes. See page 2, full paragraph 1. When the interruption of blood flow limits the oxygen supply to the proximal tubular cells of the kidney the cells may become irreversibly injured and the ensuing inflammatory responses to this initial injury provide additional insult to the

affected tissue (page 3, full paragraph 1). Where the patient suffers from a chronic inflammatory disease, such as diabetes, the morphogen preferably is administered at regular intervals as a prophylactic (page 13, lines 23-29). OP1 is among the morphogens useful in this invention (page 14, lines 1-3). OP1 (page 14, line 30, through page 15, line 17) inhibits the adherence of LTB4 activated PMNs to endothelium (Example 5, pages 74-75), inhibits cellular and humoral inflammatory reactions (Example 7, pages 78-80). Kuberasampath is silent with respect to the administration of OP1 to a mammal afflicted with chronic diabetic nephropathy.

Watanabe (x18) teaches that neutrophilic polymorphonuclear leukocytes are important effector cells in glomerular diseases, including diabetic nephropathy (page 209, column 1, full paragraph 1).

Glassock (v6) teaches that monocytes (macrophages) are present in large numbers in the glomerulus and interstitium in many forms of glomerulonephritis and tubulointerstitial nephritis; interference with the accumulation of these cells within the kidney may ameliorate the clinical and morphological manifestations of the disease (paragraph bridging pages 1294-1295).

Watanabe and Glassock do not teach the administration of OP1 to a mammal afflicted with chronic diabetic nephropathy. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer OP1 at regular intervals as a prophylactic to a patient suffering from a chronic inflammatory disease, such as diabetes, as taught by Kuberasampath, and to modify that teaching by treating a patient afflicted with chronic diabetic nephropathy, as taught by Watanabe, with a reasonable expectation of success. One of ordinary skill in the art would be

motivated to combine these teachings in order to inhibit the adherence of PMNs to endothelium, and thereby limit the progression of diabetic nephropathy and ameliorate the clinical and morphological manifestations of the disease. One of ordinary skill in the art would have a reasonable expectation that limiting the progression of diabetic nephropathy and ameliorating the clinical and morphological manifestations of the disease would cause a clinically significant improvement in a standard marker of renal function such that the mammal's need for chronic dialysis is delayed or reduced.

Kuberasampath (BB, cited by Applicants), Watanabe (x18), and Glassock (v6) provide a teaching, suggestion, or motivation to treat chronic diabetic nephropathy with OP-1.

One of ordinary skill in the art would have a reasonable expectation of success because Glassock (v6) teaches that monocytes (macrophages) are present in large numbers in the glomerulus and interstitium in many forms of glomerulonephritis and tubulointerstitial nephritis; interference with the accumulation of these cells within the kidney may ameliorate the clinical and morphological manifestations of the disease (paragraph bridging pages 1294-1295).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
AUGUST 15, 2003